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EXAMINER	
NEPVEUX, FELIX JOSEPH	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,744	HOLMAN, ANDREW	
	Examiner	Art Unit	
	Felix J. Nepveux	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13,15-22,24-26,28,29 and 40-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13,15-22,24-26,28,29 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

This Office Action is in response to the remarks and amendments filed August 31, 2004, wherein Applicant made an election of Group I with traverse. Applicant further made three species elections within Group I, which now encompasses a method of sparing an effective amount of a therapeutic agent administered to a subject having **rheumatoid arthritis** by administering to a subject an effective amount of a sleep restorative agent, wherein the therapeutic agent is **prednisone** and the sleep restorative agent is **pramipexole** (2-amino-4,5,6,7-tetrahydro-6-(propylamino)benzo-thiazole or the (-)-enantiomer thereof.

Claims 10-12, 14, 23, 27, 44, and 45 are withdrawn from further consideration as they are drawn to a nonelected species. Claims 44 and 45 are withdrawn because they are drawn to another therapeutic agent that was not elected. Claims 30-39 had been previously canceled. Claims 1-9, 13, 15-22, 24-26, 28, 29, and 40-43 are pending and are herein examined on the merits in so far as they read on the elected species of Group I and are subject to the restriction requirements filed on October 9, 2003.

Response to Arguments

Applicant's arguments filed August 31, 2004, with respect to the restriction of sleep restorative agents and sleep restorative agents that reduce the amount of therapeutic agent need for treatment of arthritis, have been fully considered and are

persuasive. This restriction requirement is now withdrawn and does not affect or alter Applicant's prior election of species and designation of claims 1-9, 13, 15-22, 24-26, 28, 29, and 40-45 as reading on the elected species. Note that claims 44 and 45 are withdrawn. The restriction requirements are now **final**.

Claim Objections

Claim 43 is objected to because of the following informalities:

(1). The therapeutic agent Trazodone, as written in the specification, was misspelled as "Trazedone" in claim 43. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "an undesired side effect" and "a side effect" are vague and indefinite because the specification recites any number of undesired side effects. Therefore, the metes and bounds of the claims cannot be ascertained by one of ordinary skill in the art.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a side effect" is vague and indefinite because the

specification recites any number of side effects. Therefore, the metes and bounds of the claims cannot be ascertained by one of ordinary skill in the art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 13, 15-22, 24-26, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for sparing an effective amount of a therapeutic agent administered to a subject **having an autoimmune condition** such as rheumatoid, Psoriatic arthritis, Systemic Lupus Erythematosis, ocular and articular Sarcoidosis, Palindromic Rheumatism, Sjogren's Syndrome, Behcet's Syndrome, Anklyosing Spondylitis, Reiter's Syndrome, chronic gout, pseudogout, and Multiple Sclerosis by administering a sleep restorative agent, **does not reasonably provide enablement for treatment of all autoimmune conditions or disorders**, such as Hashimoto's thyroiditis, Hepatitis C arthritis, and Whipple's Disease, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to In re Wands, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set

forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***The Nature of the Invention:***

The rejected claims are drawn to an invention, which pertains to a method of decreasing the effective amount of a therapeutic agent administered to a subject having an autoimmune condition by administering a sleep restorative agent. The nature of the invention is complex in that it encompasses the treatment of **numerous types of autoimmune conditions** by administering an array of combinations of a therapeutic agent and a sleep restorative agent.

(2). ***Breadth of the Claims:***

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The method of treating an autoimmune condition encompasses administering various structurally distinct therapeutic agents concomitantly with either various substituted benzo-thiazoles or structurally distinct compounds, which function as the sleep restorative agent. There are multiple possible

combinations of sleep restorative agents and therapeutic agents for the treatment of the **numerous types of autoimmune conditions** claimed.

(3). ***State of the Art:***

While it is known that some drugs are useful for treating multiple autoimmune diseases, other drugs are not as versatile. Christodoulos et al. teaches that minocycline can be used to treat rheumatoid arthritis, but can also lead to drug-induced lupus, another autoimmune disease for example (*Chest.* 1999, 115(5): 1471)

(4). ***Predictability of the Art:***

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered to be an unpredictable factor. See *in re Fisher*, 427 F.2d 833,839 (1970. The art is unpredictable because the treatment of one type of autoimmune condition will not necessarily be the same for the other type.

(5). ***Guidance of the Specification:***

The guidance given by the specification as to how to treat autoimmune diseases in general is limited. For example, guidance provided by the specification is directed toward the treatment of specific autoimmune diseases such as rheumatoid arthritis and Psoriatic arthritis by administering prednisone or methotrexate concomitantly with a sleep restorative agent. The specification does not give guidance for the treatment of Hashimoto's thyroiditis, for example.

(6). ***Working Examples:***

For example, Applicant provides *in vivo* examples of the treatment of rheumatoid arthritis and Psoriatic arthritis by administering combinations of specific therapeutic agents and sleep restorative agents. However, there is a lack of working examples to bolster all the generic claims.

(7). ***The Quantity of Experimentation Necessary:***

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an autoimmune condition, therapeutic agent, and sleep restorative agent. One would then need to test the combination in the model system to determine whether or not the combination is effective for decreasing the amount of therapeutic agent needed to treat an autoimmune disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding sparing the amount of therapeutic agent administered to a patient with an autoimmune disease by administering a sleep restorative agent, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compounds, compound dosage, duration of treatment, route of administration, etc. and appropriate model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of an autoimmune disease, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of autoimmune disease because, as shown by

Christodoulos et al., some drugs will not necessarily treat all types of autoimmune conditions. Therefore, it would require undue experimentation to practice the claimed invention of decreasing the effective amount of a recited therapeutic agent administered to a subject having an autoimmune condition by administering one of the various sleep restorative agent recited in the claims.

Genetech, 108F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and [p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.

Therefore, a method for decreasing the effective amount of various therapeutic agents administered to a subject having an autoimmune disease by co-administering various sleep restorative agents is not considered to be enabled by the instant specification.

Claims 1-8, 13, 15-22, 24-26, 28, 29, and 40-42 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the use of some sleep restorative agents, **does not reasonably provide enablement for the use of all sleep restorative agents**. For example, the specification gives support for the use of pramipexole, Lorazepam, Clonazepam, Tizanidine, Gabapentin, ropinirole, and Trazedone, while the specification does not provide enablement for the use of Zaleplon, Zolpidem, or pregabalin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to In re Wands, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***The Nature of the Invention:***

The rejected claims are drawn to an invention, which pertains to a method of treating a patient with an autoimmune disease using a combination of a therapeutic agent and a sleep restorative agent. The nature of the invention is complex in that it encompasses the treatment of many types of autoimmune diseases by administering an array of combinations of a therapeutic agent and **one of the many disclosed sleep restorative agents**.

(2). ***Breadth of the Claims:***

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The method of treating an autoimmune condition encompasses administering various structurally distinct therapeutic agents

concomitantly with either **various substituted benzo-thiazoles or structurally distinct compounds,** which function as the sleep restorative agent. There are multiple possible combinations of sleep restorative agents and therapeutic agents for the treatments claimed.

(3). ***State of the Art:***

The state of the art is low with regards to treating an autoimmune disease **by administering any sleep restorative agent**. While it is known that some drugs are useful for treating multiple autoimmune diseases, other drugs are not as versatile. For example, Christodoulos et al. teaches that minocycline can be used to treat rheumatoid arthritis, but can also lead to drug-induced lupus, another autoimmune disease (*Chest.* 1999, 115(5): 1471)

(4). ***Predictability of the Art:***

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered to be an unpredictable factor. See *in re Fisher*, 427 F.2d 833,839 (1970). Jones et al. teaches "insomnia is a problem with complex and multifactorail etiologies that requires both standardized and individualized treatment interventions." Therefore the art is unpredictable with respect to which sleep agent would be appropriate for the treatment of insomnia.

(5). ***Guidance of the Specification:***

The guidance given by the specification as to how to treat autoimmune diseases in general is limited. For example, the guidance provided by the specification is directed toward the treatment of specific autoimmune diseases such as rheumatoid arthritis and Psoriatic arthritis by administering prednisone or methotrexate concomitantly with a pramipexole. The specification does not give guidance for the treatment of Hashimoto's thyroiditis, Hepatitis C arthritis, and Whipple's Disease for example.

(6). ***Working Examples:***

Applicant provides *in vivo* examples of the treatment of rheumatoid arthritis and Psoriatic arthritis by administering combinations of specific therapeutic agents and sleep restorative agents for example. However, there is a lack of working examples to bolster all the generic claims.

(7). ***The Quantity of Experimentation Necessary:***

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an autoimmune condition, therapeutic agent, and sleep restorative agent. One would then need to test the combination in the model system to determine whether or not the combination is effective for decreasing the amount of therapeutic agent needed to treat an autoimmune disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding sparing the amount of therapeutic agent administered to a patient with an autoimmune disease by administering a sleep restorative agent, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compounds, compound dosage, duration of treatment, route of administration, etc. and

appropriate model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of an autoimmune disease, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of autoimmune disease because, as described by Christodoulos et al., some drugs will not necessarily treat all types of autoimmune conditions. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of decreasing the effective amount of a recited therapeutic agent administered to a subject having an autoimmune condition by administering one of the sleep restorative agent recited in the claims.

Genetech, 108F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and [p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.

Therefore, a method for decreasing the effective amount of various therapeutic agents by administered to a subject having an autoimmune disease by administering various sleep restorative agents is not considered to be enabled by the instant specification.

Claims 1-9, 13,15-22, 24-26, 28, 29, 40, 41, and 43 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while

being enabling for the use of some therapeutic agents, **does not reasonably provide enablement for the use of all therapeutic agents**. For example, the specification enables the use of prednisone, but it is not enabled for the use of any immunomodulatory agent as recited in claim 19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 13 is rejected because Applicant employs functional language to define the claim. In the instant case, the term "immunosuppressive monoclonal antibodies to a leukocyte receptor" encompasses any number of antibodies. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty." Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate." Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the

patent of the limits of the monopoly asserted" *General Electric Company v. Wabash Appliance Corporation et* supra, at 468. Claims thus constructed provide no guidance as to medicaments employed, levels for providing therapeutic benefit, or provide notice for those practicing in the art, limits of protection. Simply stated, the presented claims are an invitation to experiment, not reciting a specific medicament regimen useful for practicing the instant invention.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to In re Wands, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***The Nature of the Invention:***

The rejected claims are drawn to an invention, which pertains to a method of treating a patient with an autoimmune disease using a combination of a therapeutic agent and a sleep restorative agent. The nature of the invention is complex in that it

encompasses the treatment of many types of autoimmune diseases **by administering an array of combinations of a therapeutic agent** and a sleep restorative agent.

(2). ***Breadth of the Claims:***

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The method of treating an autoimmune condition encompasses administering various structurally distinct therapeutic agents, including prednisone, methotrexate, Interferon-Beta-1b, and Hydroxychlorquine for example, concomitantly with either various substituted benzo-thiazoles or structurally distinct compounds, which function as the sleep restorative agent. There are multiple possible combinations of sleep restorative agents and therapeutic agents for the treatments claimed.

(3). ***State of the Art:***

The state of the art is low with regards to treating an autoimmune disease by decreasing the effective amount of therapeutic agent by administering a sleep restorative agent. While it is known that some drugs are useful for treating multiple autoimmune diseases, other drugs are not as versatile. For example, Christodoulos et al. teaches that minocycline can be used to treat rheumatoid arthritis, but can also lead to drug-induced lupus, another autoimmune disease (*Chest.* 1999, 115(5): 1471)

(4). ***Predictability of the Art:***

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered

to be an unpredictable factor. See *in re Fisher*, 427 F.2d 833,839 (1970). The treatment of one type of autoimmune condition will not necessarily be the same for the other type.

(5). ***Guidance of the Specification:***

The guidance given by the specification as to how to treat autoimmune diseases in general is limited. For example, the guidance provided by the specification is directed toward the treatment of specific autoimmune diseases such as rheumatoid arthritis and Psoriatic arthritis by administering prednisone or methotrexate concomitantly with a pramipexole. The specification does not give guidance for the treatment of Hashimoto's thyroiditis, Hepatitis C arthritis, and Whipple's Disease for example.

(6). ***Working Examples:***

Applicant provides *in vivo* examples of the treatment of rheumatoid arthritis and Psoriatic arthritis by administering combinations of specific therapeutic agents and sleep restorative agents for example. Therefore, there is a lack of working examples to bolster all the generic claims.

(7). ***The Quantity of Experimentation Necessary:***

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an autoimmune condition, therapeutic agent, and sleep restorative agent. One would then need to test the combination in the model system to determine whether or not the combination is effective for decreasing the amount of therapeutic agent needed to treat an autoimmune disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding

sparing the amount of therapeutic agent administered to a patient with an autoimmune disease by administering a sleep restorative agent, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compounds, compound dosage, duration of treatment, route of administration, etc. and appropriate model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of an autoimmune disease, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of autoimmune disease because, as described by Christodoulos et al., some drugs will not necessarily treat all types of autoimmune conditions. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of decreasing the effective amount of a recited therapeutic agent administered to a subject having an autoimmune condition by administering one of the sleep restorative agent recited in the claims.

Genetech, 108F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and [p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.

Therefore, a method for decreasing the effective amount of <u>various</u> therapeutic agents by administered to a subject having an autoimmune disease by administering

various sleep restorative agents is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

Claims 1-9, 13, 15-22, 24-26, 28, 29, and 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lapin (US 4,743,596) in view of Wojtulewski et al. (*Curr. Med. Res. and Opin*. 1983, 8(7)) and Monti et al. (*European Neuro-psychopharmacology*, 1998, 8(2)).

Lapin teaches a method of treating rheumatoid arthritis by administering prednisone as a therapeutic agent (column 2, line 14-17, for example).

Lapin does not teach a method of treating rheumatoid arthritis by administering a composition comprising prednisone and pramipexole as a sleep restorative agent.

Wojtulewski et al. teaches that insomnia is a secondary condition of rheumatoid arthritis (page 456, for example).

Monti et al. teaches a method of treating sleep disorders by administering pramipexole as a sleep restorative agent. In an animal study during the first hour of recording, a 30 μg/kg dose of pramipexole was shown to decrease wakefulness and increase slow wave sleep and REM (page 155, table 1, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine prednisone with pramipexole for the treatment of rheumatoid arthritis.

One of ordinary skill in the art would have been motivated to combine pramipexole with prednisone in the treatment of rheumatoid arthritis because **(1)** Lapin teaches a method of treating rheumatoid arthritis with prednisone as a therapeutic agent, **(2)** Wotulewski teaches that insomnia is a secondary condition of rheumatoid arthritis, and **(3)** Monti et al. teaches that pramipexole can be administered as a sleep restorative agent for the treatment of insomnia. Since pramipexole is known to be useful in treating insomnia, which is a well-known secondary condition of rheumatoid arthritis, the use of pramipexole to treat insomnia would be considered to be one of the treatments for rheumatoid arthritis since the symptoms are overlapping for both diseases. Concomitant employment of both prednisone and pramipexole in a method to treat rheumatoid arthritis would have been reasonably expected to be effective, with at least an additive effect, since both prednisone and pramipexole are known to be useful to treat rheumatoid arthritis separately. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Felix J. Nepveux whose telephone number is (571) 272-8514. The examiner can normally be reached on m-f 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Felix J. Nepveux V

FJN

SAN-MING HU
PRIMARY EXAMINER